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Electronic Supplementary Material

Consideration of the bioavailability of metal/metalloid species in freshwaters: experiences regarding the implementation of biotic ligand model-based approaches in risk assessment frameworks

Heinz Rüdel*, Cristina Díaz Muñiz, Hemda Garelick, Nadia G. Kandile, Bradley W. Miller, Leonardo Pantoja Munoz, Willie J. G. M. Peijnenburg, Diane Purchase, Yehuda Shevah, Patrick van Sprang, Martina Vijver, Jos P.M. Vink

* corresponding author: Heinz Rüdel, Fraunhofer Institute for Molecular Biology and Applied Ecology (Fraunhofer IME), Auf dem Aberg 1, 57392 Schmallenberg, Germany; e-mail Heinz.Ruedel@ime.fraunhofer.de; Tel. +49 2972 302 301

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Publications which consider the bioavailability of metals/metalloids species in the aquatic environment

Table S1: BLMs for studying chronic and acute metal toxicity - literature evaluation (period ca. 2000 - 2013). WQC - water quality criteria; DOC – dissolved organic carbon; DOM – dissolved organic matter

Metal(s)/ Metal-loid(s)	**Test organism(s)**	**Chronic/ acute expo-sure (C/A)**	**Cations**	**Other ligands / factors**	**Notes**	**Reference**
Ag nano-particles	*Ceriodaphnia dubia* (freshwater zooplankton)	A	Ca^{2+}, Na^{+}	DOC	BLM predictions based on the dissolved fraction in nano-silver suspensions were comparable to observed toxicity; application of BLM for hypothesis testing, use of available model	Kennedy et al. (2012)
Ag nano-particles	*Nitrifying bacteria*	A		SO_4^{2-}, S^{2-}, Cl^{-}, PO_4^{3-}, EDTA	S^{-} was the only ligand to effectively reduce nanosilver toxicity. BLM was successful in predicting Ag^{+} toxicity BUT it was not	Choi et al. (2009)

Metal(s)/ Metal-loid(s)	Test organism(s)	Chronic/ acute exposure (C/A)	Cations	Other ligands / factors	Notes	Reference
					accurate for Ag nanoparticles in wastewater.	
Ag	*Ceriodaphnia dubia* (freshwater zooplankton)	A		DOM	BLM-calculated toxicity could be improved by incorporating specific chemical constituents of DOM.	Kolts et al. (2008)
Ag	*Pseudokirchneriella subcapitata* and *Chlamydomonas reinhardtii* (freshwater algae)	A		Cl^-	BLM able to predict growth inhibition based on the metal intracellular quota in relation to Cl^-, indicating that Ag toxicity was due to cell accumulation rather than surface interaction.	Lee et al. (2005)
Ag	*Oncorhynchus mykiss* (rainbow trout)	A	Ca^{2+}, Na^+, Mg^{2+}	Cl^-	Evidence to support using BLM to predict Ag toxicity; application of BLM for hypothesis testing, use of available model	Morgan and Wood (2004)
Ag	*Oncorhynchus mykiss* (rainbow trout)	A			BLM together with interaction of water chemistry on the physiological condition of the organisms were incorporated into a model to predict survival time for rainbow trout when exposure to Ag.	Paquin et al (2002)
Ag	*Oncorhynchus mykiss* (rainbow trout), Cambarus diogenes (crayfish), Daphnia magna	A	Na^+, K^+		Na^+ uptake rate should be incorporated in BLM to improve its predictability. In the absence of Na^+ uptake rate, body mass may be used as a substitute.	Bianchini et al (2002)

Metal(s)/ Metal-loid(s)	Test organism(s)	Chronic/ acute expo-sure (C/A)	Cations	Other ligands / factors	Notes	Reference
Ag	*Oncorhynchus mykiss* gill epithelial cells	A	Na^+, K^+, Ca^{2+}	Transepithelia resistance, transepithelial potential, DOC, Cl^-, pH	With the exception of pH response, the *in vitro* BLM behaved qualitatively and quantitatively similar to in vivo BLM; epithelial gill cells may provide a cost-effective alternative.	Zhou et al (2005)
Ag	*Chlamydomonas reinhardtii, Pseudokirchneriella subcapitata*	A		thiosulfate	BLM was used to assess the uptake and toxicity of Ag in the presence of inorganic ligand and thiosulfate. Results suggest that the $Ag(S_2O_3)^-$ complex remains at least partially intact in the intracellular environment, limiting the internal bioavailability of Ag.	Hiriart-Baer et al. (2006)
Ag	*Daphnia magna*	C	Na^+		The key mechanism involved in chronic Ag toxicity is similar to acute toxicity; Na^+ uptake inhibition is the best endpoint; possibility to extend the acute version of BLM to predict chronic toxicity.	Bianchini and Wood (2002)
Ag	*Daphnia magna*	A+C		S^{2-}, water hardness	Both reactive S^{2-} and water hardness must be taken into account in the development of chronic BLM for Ag.	Bianchini and Wood (2008)
Ag	*Daphnia magna*	A	Na^+, K^+		Mechanism of Ag toxicity in *D. magna* was similar to freshwater fish. BLM for rainbow trout achieves the correct sensitivity for daphnids by reducing the saturation of toxic sites needed to cause toxicity.	Bianchini and Wood (2003)

Metal(s)/ Metal-loid(s)	Test organism(s)	Chronic/ acute expo-sure (C/A)	Cations	Other ligands / factors	Notes	Reference
Ag	*Daphnia magna*, *D. pulex*, *Gammarus pulex*	A	Na^{+}, K^{+}, Ca^{2+}	Cl^{-}, organic thiols, thiosulfate	The derived daphnid BLM did not accurately predict *G. pulex* toxicity and had limited success when applied to waters containing organic thiols or thiosulfate.	Bury et al (2002)
Ag	*Acartia tonsa* (copepod*)*	A	Na^{+}, K^{+}, Mg^{2+}, Ca^{2+}	Presence and absence of food; salinities; Cl^{-}, $SO4^{2-}$, DOC	Acute Ag toxicity was salinity dependent (decreased as salinity increased); dietary intake affected the toxicity. Future BLM needs to incorporate both salinity and food for estuarine and marine conditions for *A. tonsa*.	Pedroso et al. (2007)
Ag	*Penaeus duorarum (*shrimp*), Aplysia californica (*sea hare*), Diadema antillarum* (sea urchin*)*	A	Na^{+}, K^{+}, Ca^{2+}, Mg^{2+}	Cl^{-}	Ag toxicity did not affect osmotic or ionoregulation at the hemolymph level in marine organisms; toxicity affected water and ion regulation in cellular level in different tissues. BLM for seawater should consider other ligands in addition to gills	Bianchini et al. (2005)
Ag, Cd	*Chlamydomonas reinhardtii*, *Pseudokirchneriella subcapitata*	A		Cl^{-}, NO^{3-}, SO_4^{2-}, $S_2O_3^{2-}$	Genreally, BLM performed crediably except in the presence of alanine or thiosulfate and where the metal-sensitive site is present on the outer surface of the target organism	Campbell et al (2002)
Ag, Cu				S^{2-}	The papers argued that S^{2-} species should be accounted for	Bell et al. (2002), Bianchini and Bowles (2002)

Metal(s)/ Metal-loid(s)	Test organism(s)	Chronic/ acute expo-sure (C/A)	Cations	Other ligands / factors	Notes	Reference
Ag, Cd, Cu, Zn	Marine fish, molluscs and Daphnids	A	Ca^{2+}, Na^{+}		BLM and bioaccumulation kinetics aremerged into a common mechanistic framework for Metal uptake in aquatic organisms, a new aproach is proposed to combine effect of metal chemodynamics, ligand affinity and species characteristics	Veltman et al. (2010)
As	*Corbicula fluminea* (freshwater clam)	A	Ca^{2+}, Na^{+}		Application of BLM and damage assessment model to examine ecophysiological response of *C. Fluminea:* higher As binding in gill biotic ligand at 50% mortality level gives a lower capacity to accumulate bioavailable As	Chen and Liao (2010)
As	*Oreochromis mossambicus (*tilapia*)*				Application of BLM and damage assessment model to develop a toxicokinetic model for As bioavailability	Tsai et al. (2009)
As	*Oreochromis mossambicus* (tilapia)	A			A BLM-based approach to predict both acute and chronic effects of As concentration on tilapia	Chen et al (2009)
Cd	*Chlamydomonas reinhardtii*	C	Fe^{3+}, Mn^{2+}, Ca^{2+}, Zn^{2+}, Co^{2+}	Nitrilotriacetic acid	BLM predicted increase of Ca^{2+} offered protection of Cd toxicity; essential trace metal concentrations may strongly affect the uptake and toxicity of Cd in *C. reinhardtii*; study recommends improvement of Cd BLM	Lavoie et al. (2012a)

Metal(s)/ Metal-loid(s)	Test organism(s)	Chronic/ acute expo-sure (C/A)	Cations	Other ligands / factors	Notes	Reference
Cd	*Daphnia pulex*	A	Na^{+}, Mg^{2+}, Ca^{2+}, K^{+}, H^{+}	DOC,Cl^{-}	HydroQual BLM v. 2.2.3 applied to predict acute Cd toxicity; a modified BLM specific for *D. Pulex* was developed to take into account of the moderating effect of Ca and Mg and DOC	Clifford and McGeer (2010)
Cd	*Photobacterium phosphoreum*	A	Ca^{2+}, Mg^{2+}, K^{+}	pH, complexants (EDTA, commercial DOM, homemade DOMs)	Cd toxicity was enhanced at larger K^{+} concentration; a toxicity alleviation by H^{+} was observed over the tested pH range of 5.0-9.0; additions of complexants reduced Cd bioavailability; all factors were finally incorporated into a specific BLM for *P. phosphoreum*	Qu et al. (2013)
Cd	*Perca flavescens* (yellow perch), *Oncorhynchus mykiss* (rainbow trout)	A	Ca^{2+}		The acute Cd BLM could not be extended from rainbow trout to yellow perch by adjustments of LA50 values. Ca^{2+} and Cd pre-exposure also affected Cd and Ca bonding in fish gills. Future refinement of the acute Cd BLM was recommended	Niyogi et al. (2004)
Cd	*Oncorhynchus mykiss* (rainbow trout)	A	Ca^{2+}, Mg^{2+}, Na^{+},	pH, alkalinity, DOC	A BLM was developed to predict toxicity of Cd in rainbow trout with good accuracy except for high alkalinity and pH	Niyogi et al (2008)
Cd	*Oncorhynchus mykiss* (rainbow trout)	C		Dietary route of exposure	The route of Cd exposure (dietary or water-borne) affected the internal Cd accumulation and branchial Cd uptake. Furture BLM should consider the route of Cd exposure	Szebedinszky et al (2001)

Metal(s)/ Metal-loid(s)	Test organism(s)	Chronic/ acute expo-sure (C/A)	Cations	Other ligands / factors	Notes	Reference
Cd, Mn	*Chlamydomonas reinhardtii*	A	Ca^{2+}	pH	Mn and Cd biological internalisation was of first order but maximum transport flux contradicts the BLM (decreased when pH decreased), suggesting non-competitive inhibition of metal uptake by H^+; therefore, the current BLM did not reflect effect of H^+ on Mn and Cd by algae	Francois et al. (2007)
Cd, Pb		A	Ca^{2+}		BLM-based approach to predict Cd/Pb mixture toxicity from the single metal toxicity data	Jho et al. (2011)
Cd+Pb	*Oncorhynchus mykiss* (rainbow trout)	A	Ca^{2+}, H^+, Na^+	NOM	Cd and Pb mixture caused a reduction in metal-gill binding but exacerbated ionic disturbances in soft and moderately acidic waters; the BLM for fish should be re-evaluated in water containing metal mixtures	Birceanu et al. (2008)
Cd, Zn	*Chlamydomonas reinhardtii*	C + A			BLM developed to incorporate the effects of both chemical speciation and physiological regulation of Cd transport system	Lavoie et al. (2012b)
Cd, Zn	*Microcystis aeruginosa*	A + C		EDTA, NTA	Intracellular Cd or Zn was more effective in explaining acute and chronic metal toxicity; BLM may be used to predict Cd or Zn toxivity in *M. aeruginosa*	Zeng et al (2009)

Metal(s)/ Metal-loid(s)	Test organism(s)	Chronic/ acute expo-sure (C/A)	Cations	Other ligands / factors	Notes	Reference
Cd, Cu, Pb and Zn			Ca^{2+}, Mg^{2+}, Na^{+}, K^{+}	pH, DOC, SO_4^{2-}	The choice of model (WHAM VI, NICA-Donnan and SHM) that defines metal/organic-matter interactions had little effect on predicted dissolved Cd or Zn speciation and Cd/ or Zn/biotic-ligand concentrations; but the choice influenced the predicted dissolved Cu and Pb speciation and Cu/ or Pb/biotic-ligand concentrations	Balistrieri and Blank (2008)
Cu	*Lampsilis siliquoidea* (freshwater mussels)	C	Na^{+}, K^{+}	-	The US EPA BLM-derived chronic WQC and the hardness-derived WQC both underprotect juvenile *L. siliquoidea*; no further application of BLM approach	Jorge et al. (2013)
Cu	*Lampsilis siliquoidea, Lampsilis fasciola*	A		DOC (8 natural waters)	DOC offered significant protection to mussel larve to Cu toxicity; need to be considered in the BLM	Gillis et al. (2010)
Cu	*Scenedesmus subspicatus* (freshwater alga)	A		EDTA, fulvic acid	Both EDTA and fulvic acid reduced Cu toxicity; Cu toxicity was related to a biotic ligand at algal cell wall. The results suggested BML could be extended to predict the influence of Cu on growth inhibition of alga	Ma et al. (2003)
Cu	*Daphnia magna*	C	-	-	Dietary exposure of Cu it did not affect the predictive capacity of the BLM	De Schamphelaere and Janssen (2004a)

Metal(s)/ Metal-loid(s)	Test organism(s)	Chronic/ acute expo-sure (C/A)	Cations	Other ligands / factors	Notes	Reference
Cu		A	H^+	Ratio Cu/DOM; binding constants	Compared with the speciation modelVisual MINTEQ; BLM was found to overestimate Cu^{2+} at lower total Cu concentration but underestimate Cu^{2+} at high total concentration	Craven et al. (2012)
Cu	*Daphnia magna*	A	Ca^{2+}, Mg^{2+}, Na^+, K^+, H^+		Results suggested co-toxicity of $CuOH^+$ rather than H^+ competition; a BLM was developed to predict acute Cu toxicity as a function of these water characteristics including $CuOH^+$	De Schamphelaere and Janssen (2002)
Cu	*Daphnia magna*	C	Ca^{2+}, Mg^{2+}, Na^+, H^+	DOC, DOM	A specific absorption coefficient as a DOM quality indicator was incorporated into a BLM to increase accuracy for predicting Cu toxicity	Al-Reasi at al. (2012)
Cu	*Daphnia magna*	A/C	Ca^{2+}, Mg^{2+}, Na^+, H^+		Usage of acute Cu BLM to predict chronic Cu toxicity to *D. magna;* BLM modified by adjusting the accumulation associated with 50% of an effect value	Villavicencio et al. (2011)
Cu	*Daphnia magna*	C	Ca^{2+}, Na^+, H^+	H^+, DOM, water hardness, DOC	All investigated parameters affected the BLM outcome and should be adjusted on base of the study data to improve accuracy of the model	Ryan et al. (2009)
Cu	*Daphnia magna, D. pulex and D. obtuse*	A	Ca^{2+}, Na^+, H^+	DOC	Use of acute Cu BLM with different parameter sets to predict toxicity to daphnids in a range of natural waters in Chile; BLM can be applied to most low-DOC waters; for high-DOC waters, US EPA criteria were overprotective	Villavicencio et al. 2005

Metal(s)/ Metal-loid(s)	Test organism(s)	Chronic/ acute expo-sure (C/A)	Cations	Other ligands / factors	Notes	Reference
Cu	*Daphnia magna*, *Mytilus edulis*	A/C			Application of existing Cu BLM to estimate the potential magnitudes and variabilities of bioavailable Cu in fresh surface water from different regions of the world	Van Genderen et al (2008).
Cu	*Hyalella azteca*	A	Ca^{2+},Mg^{2+}, Na^{+}, K^{+}	pH	The developed BLM can be applied to fish and *Daphnia* (with different coefficients)	Borgmann et al. (2005)
Cu	*Oncorhynchus mykiss* (rainbow trout), *O. tsha-wytscha* (Chinook salmon), *O. kisutch* (coho salmon) and *Pimephale spromelas* (fathered minnows)	A + C			A Cu-olfactory BLM was parameterized by changing the sensitivity parameter in the ionoregulatory-based BLM; US EPA BLM-based WQC for Cu protects against neuro-physiological impairment of these fish but the hardness-based criteria underprotects them	Meyer and Adams (2010)
Cu	Fish	A + C			Considerations for development of a Cu BLM for marine/estuarinewaters; for marine fish intestine should be considered as biotic ligand;the osmotic gradient should also be consideredfor BLM calculations	De Polo and Scrimshaw (2012)
Cu	*Oncorhynchus mykiss* (rainbow trout)	A + C	Ca^{2+}, Mg^{2+}, H^{+}	Soft water	BLM did not adequately predict Cu toxicity to trout in soft water	Ng et al. (2010)
Cu	*Oncorhynchus mykiss* (rainbow trout)	A	Ca^{2+}, Na^{+}, Mg^{2+}, K^{+}	NOM (3 different sources and quality)	BLM consistently underestimated Cu-gill binding; the data suggested variability in toxicity was due to direction actions of NOM on gills which were quality dependent	Gheorghiu et al. (2010)

Metal(s)/ Metal-loid(s)	Test organism(s)	Chronic/ acute expo-sure (C/A)	Cations	Other ligands / factors	Notes	Reference
Cu	*Pimephales promelas* (fathead minnows)	A			BLM was combined with a one-compartment uptake-depuration model to predict the acute toxicity of continuous and pulse exposure of Cu to fathead minnows	Meyer et al. (2007)
Cu	*Perca flavescens* (yellow perch), *Oncorhynchus mykiss* (rainbow trout)	A			The BLM could not be extended from rainbow trout to yellow perch; future refinement of the acute Cu BLM for each species was recom-mended	Pyle and Wood (2008)
Cu	*Pimephales promelas* (fathead minnows), Daphnia	A	Ca^{2+}	NOM, water hardness	A Cu BLM was developed to calculate LC50 which compared well with published data	Santore et al. (2001)
Cu	*Cnesterodon decemmaculatus* (ten-spotted live-bearing fish)	A	Na^{+}, Ca^{2+}, Mg^{2+}	SO_4^{2-}, Cl^{-}	A higher protective effect of Ca, Mg, Na, sulfate and chloride is expected during the dry season; across-fish-species extrapolation of BLM was feasible	Casares et al. (2012)
Cu	*Fundulus heteroclitus* (killifish)	A+C		Salinity	The gills accumulated more Cu at lower sali-nities but the intestine accumulated more at higher salinities; seawater BLM should con-sider potential target tissues in addition to gills	Blanchard and Grosell (2005)
Cu	*Acartiatonsa* (copepods)	A		Presence and absence of food and salinity	High salinity (30 parts per thousand, ppt) reduced Cu toxicity; availability of food exerted an important positive impact in protection against Cu toxicity; future BLM needs to incorporate both salinity and food for	Leaes Pinho and Bianchini (2010)

Metal(s)/ Metal-loid(s)	**Test organism(s)**	**Chronic/ acute expo-sure (C/A)**	**Cations**	**Other ligands / factors**	**Notes**	**Reference**
					Cu toxicity in estuarine and marine waters; *A. tonsa*seems seems to be a suitable model species for saltwater BLM	
Cu	*Acartia tonsa* (euryhaline copepod)	A		DOM	Both salinity (30 ppt) and DOM should be taken into account in the development of an estuarine version of the BLM	Rodrigues Monteiro et al. (2013)
Cu	*Lemna aequinoctialis*	A	Ca^{2+}, Mg^{2+}, Na^{+}, K^{+}	Cl^{-}, SO_4^{2-}, pH DOM	The BLM approach can be used to accurately predict short-term metal toxicity to *L. aequinoctialis* as a function of water quality characteristics	Shoji (2008)
Cu	*Ceriodaphnia dubia*	C	Ca^{2+}, Na^{+}	pH, natural organic matter (NOM)	BLM developed and validated to predict Cu toxicity to *C. dubia* includes the effect of pH and NOM complexation	Schwartz and Vigneault (2007)
Cu		C	Mg^{2+}, Ca^{2+}, Na^{+}, K^{+}	Alkalinity, SO_4^{2-}, Cl^{-}	Simplification of the input requirements of the Cu BLM is proposed by estimating the concentrations of the major ions	Peters et al. (2011a)
Cu	Cladoceran species (4 different families and 11 different genera)	A		Acidity, water chemistry and water types	Bioavailability is more important thaninter-community difference in determining the variability of Cu toxicity across different aquatic systems. BLM was a generally valuable tool but more work was required for acidic surface water	Bossuyt et al. (2004)

Metal(s)/ Metal-loid(s)	Test organism(s)	Chronic/ acute expo-sure (C/A)	Cations	Other ligands / factors	Notes	Reference
Cu	Cladoceran	A	Na^{+}		Increased Na (up to 4mM) protected against Cu toxicity; results suggested processes other than Cu-Na competition at a single biotic ligand site was involved in Cu utoxicity. The data could be used to refine the BLM	De Schamphelaere et al. (2007)
Cu	*Ceriodaphnia dubia*,*Daphnia pulex* and *Pimephales promelas*	A	Ca^{2+}, Mg^{2+}, Na^{+}, H^{+}	Very hard surface water; DOC	BLM suitable to determine Cu toxicity in hard surface water; BLM generates appropriate criteria compared to the hardness-based equation or water-effect ratio approach	Van Genderen et al. (2007)
Cu	*Mytilus* sp.	C	Mg^{2+}, Ca^{2+}, Na^{+}, K^{+}, $^{-}$	Cl^{-}, SO_4^{2-}	BLM suitable to predict Cu toxicity in marine and estuarine environment	Arnold et al. (2005)
Cu	*Villosa iris (*unionid mussel*), Ceriodaphnia dubia*, *Lamsilis siliquidea*	A+C		DOC	Cu AWQC might not adequately protect the mussel from acute and chronic Cu exposure and cladoceran from chronic exposure	Wang et al (2011); Wang et al. (2009)
Cu	*Corbicula fluminea* (freshwater clam)	A			Cu binds to clam gills; Cu-BLM for – *Corbicula*can be used to describe Cu toxicity	Liao et al. (2007a)
Cu	*Corbicula fluminea*		Na^{+}		A mechanistic model (flux-biological response) based on BLM and Michaelis-Menten kinetics to link between valve closure behaviour and Na transport in response to waterborne Cu; a possible basis for a new biomonitoring tool	Liao et al. (2007b)

Metal(s)/ Metal-loid(s)	**Test organism(s)**	**Chronic/ acute expo-sure (C/A)**	**Cations**	**Other ligands / factors**	**Notes**	**Reference**
Cu	*Callinectes sapidus* (blue crab) cell line				Results support that Cu toxicity was driven by Cu accumulation in the biotic ligand (gill cells); these cells can be used as a model to develop an in vitro BLM for marine condition	Paganini and Bianchini (2009)
Cu				NOM, wastewater organic matter, S2-	Experimental Cu complexation was compared to WHAM (VI); WHAM did not reflect the Cu binding with wastewater organic matter, possibly due to the presence of nonhumic macromolecules. Future BLM should also consider alternative ligands to humic acid	Sarathy and Allen (2005).
Cu, Al				DOM, Al^{3+}	Using WHAM VI to determine the effect of DOM and Al^{3+} on Cu activity; DOM quality was an important variable and should be included in WHAM VI and BLM	Chappaz and Curtis (2013)
Cu, Cd	*Lemna paucicostata* (duck weed)	A			Toxic Unit (TU) was derived using BLM, can estimate combined toxicity of Cu and Cd	Hatano and Shoji (2008)
Cu, Ni	*Pimephales promelas (fathead minnows)*	A		Water hardness	BLM predicts acute Cu toxicity than free-ion activity for Ni or Cu in fathead minnows	Meyer et al. (1999)
Cu, Pb	*Chlamydomonas reinhardtii*	A			At high concentration (>1mM), Cu inhibits Pb transport; at low concentration, Cu had a synergistic effect on Pb uptake which confounded the BLM; bioaccumulation appeared to be much more dynamic than assumed in the equilibrium models	Chen et al. (2010)

Metal(s)/ Metal-loid(s)	Test organism(s)	Chronic/ acute expo-sure (C/A)	Cations	Other ligands / factors	Notes	Reference
Cu, Zn	*Chlorella* sp. (freshwater alga)	A	Ca^{2+}	pH	Results support the use of BLM; metal binding sites on cell surface may be a candidate as biotic ligand for a chronic BLM with microalgae	Wilde et al. (2006)
Cu, Cd, Co	*Lemna paucicostata*, *Daphnia magna*, *Oncorhynchus mykiss* (rainbow trout)	A		Exposure time	A BLM incorporating time dependency of toxicity was developed to predict toxicity of Cu, Cd and Co	Hatano and Shoji (2010)
Cu, Cd, Zn	*Oncorhynchus mykiss* (rainbow trout)	C/A			A meta-analysis of literature data of the toxicity these metals on rainbow trout using a modified BLM (incorporating proportion of non-metal binding ligand)	Kamo and Nagai (2008)
Cu, Cd, Zn	*Oncorhynchus mykiss* (rainbow trout)	C/A	Na^{+}, Ca^{2+}, Mg^{2+}, H^{+}	OH^{-}, Cl^{-}, CO_3^{2-} DOM	A meta analysis of literature data showing impact of chronic acclimation to waterborne factors, dietary composition on gill metal-binding characteristics; a more integrative approach was recommended	Niyogi and Wood (2003)
Cu, Ni, Zn		C		DOC, DOC and pH, or DOC, pH and Mg^{2+}, Ca^{2+} or Na^{+}	BLM simplified to linear equations with an acceptable level of accuracy, requiring a maximum of three measured water chemistry parameters	Verschoor et al. (2012b)

Metal(s)/ Metal-loid(s)	Test organism(s)	Chronic/ acute expo-sure (C/A)	Cations	Other ligands / factors	Notes	Reference
Cu, Ni, Zn					BLM was used to calculate average toxicity in a new method for calculating comparative toxicity of Cu, Ni and Zn in fresh water for Life Cycle Impact Analysis	Gandhi et al. (2010)
Cu, Ni, Zn	*Daphnia magna* *Gammarus roeseli*	C	Ca^{2+}, Mg^{2+}, H^{+}	DOC	Relations between bioaccumulation and fractional occupancy of the Biotic Ligand were investigated for two aquatic species under ambient field conditions	Verschoor et al. (2012a)
Hg	*Oncorhynchus mykiss* (rainbow trout)		Ca^{2+}, K^{+}	Cl^{-}, EDTA, NTA, ethylenediamine, cysteine, NOM	The study examined physiologically regulated Hg uptake from passive up take by rainbow trout; Hg has high $K_{Hg\text{-}gill}$ which suggests it was a suitable candidate for creating a BLM for inorganic Hg and fish	Klinck et al. (2005)
Mn	Fish, invertebrates and algae	C	Ca^{2+}, Mg^{2+}, H^{+}	DOC	Ca protects fish and invertebrates, Mg also protects invertebrates, and H^{+} algae; DOC had very little effect on toxicity of Mn^{2+}	Peters et al. (2011b)
Ni	*Lymnaea stagnalis* (snail), *Chironomus tentans* and *Brachionus calyciflorus* (rotifer);*Lemna minor*	C	Ca^{2+}, Mg^{2+}, H^{+}	DOC	BLM for *Daphnia magna*, *Ceriodaphnia dubia* was used to predict Ni toxicity to invertebrates; BLM for *Pseudokirchneriella subcapitata* and *Hordeum vulgare* to predict Ni toxicity to *L. minor*	Schlekat et al. (2010)

Metal(s)/ Metal-loid(s)	Test organism(s)	Chronic/ acute expo-sure (C/A)	Cations	Other ligands / factors	Notes	Reference
Ni	*Chironomus riparius, Lymnaea stagnalis, Lumbriculus variegatus and Daphnia pulex*	A	Ca^{2+}		Bioaccumulation and acute toxicity was tested; water hardness was protective against acute Ni toxicity; higher water hardness significantly reduced Ni bioaccumulation	Leonard and Wood (2013)
Ni	*Pseudokirchnerielia subcapitata*	A	Ca^{2+} Mg^{2+}	Water hardness	Mg and not Ca protected the alga against Ni toxicity; log K(Mg-BL) was identical for soft and hard waters; it was suggested that a single bioavailability model could be used to predict Ni toxicity in both soft and hard surface waters	Deleebeeck et al. (2009a, 2009b)
Ni	*Chlamydomonas reinhardtii*	A	H^+, Mg^{2+}, Ca^{2+}, Al^{3+}, Cu^{2+}, Zn^{2+}		Ni internalisation fluxes were linked to H^+, Mg^{2+}, Al^{3+}, Cu^{2+} and Zn^{2+}; results will contribute towards improving predictability of BLM on the stability constants of these metals	Worms and Wilkinson (2007).
Ni	*Lemna minor L.*		Ca^{2+}, Mg^{2+}, Na^+, K^+	SO_4^{2-}, Cl^-, NO_3^-	Total dissolved Ni concentration and free Ni ion activity was determined and Ni accumulation kinetics was explored; major cations did not inhibit Ni accumulation via competitive inhibition as expected by the BLM	Gopalapillai et al. 2013
Ni	*Daphnia pulex*	A	Ca^{2+}, Mg^{2+}, Na^+, K^+, H^+	Natural organic matter, Cl^-	A BLM was developed for *D. pulex* in soft water to predict Ni toxicity over a wide range; Na, K and Cl did not influence the toxicity response	Kozlova et al. (2009)

Metal(s)/ Metal-loid(s)	**Test organism(s)**	**Chronic/ acute exposure (C/A)**	**Cations**	**Other ligands / factors**	**Notes**	**Reference**
Ni	*Daphnia magna*	A		Sediments	Addition of humate attenuated Ni toxicity; organic ligands and suspended solids should be incorporated into BLM	Cloran et al. (2010)
Ni	*Daphnia magna*	A	Ca^{2+}. Mg^{2+}, Na^{+}	pH	A modified BLM (exclude log K(Na-BL), include log K(Mg-BL) and log K(Ca-BL) offered better prediction of Ni toxicity; the effect of pH required further research	Deleebeeck et al. (2008)
Ni	*Daphnia magna*	C	Ca^{2+}, Mg^{2+}	pH, DOC	DOC protected *D. magna* against chronic Ni toxicity; BLM was optimised to correct the overestimation in natural waters	Deleebeeck et al. (2008)
Ni	*Pimephales promelas*(fathead minnows)	A	Ca^{2+}, H^{+}	pH, NOM	Ni toxicity was inversely related to water hardness; the effect of pH was confounded by hardness and the presence of NOM; the BLM was not accurate at the extreme ends of pH; it may need to consider $NiCO_3$ to be bioavailable to improve its accuracy	Hoang et al. (2004)
Ni	*Oncorhynchus mykiss* (rainbow trout)	C	Ca^{2+}, Mg^{2+}	pH	The developed BLM was promising but need to take into account of the effect of pH and the mechanisms to modified Ni toxicity by Ca^{2+}, Mg^{2+} and pH need to be further explored	Deleebeeck et al. (2007)

Metal(s)/ Metal-loid(s)	Test organism(s)	Chronic/ acute expo-sure (C/A)	Cations	Other ligands / factors	Notes	Reference
Pb	*Pimephales promelas* (fathead minnows), *Ceriodaphnia dubia* (daphnids)	A	Ca^{2+}	Water hardness, DOC (humic acid), alkalinity ($NaHCO_3$)	Ca^{2+} protected acute Pb toxicity to *P. promelas* but not to *C. dubia*; DOC and alkalinity offered stronger protection to *P. promelas*. Cross-species BLM was not recommended for *P. promelas* and *C. dubia*	Mager et al. (2011a)
Pb	*Ceriodaphnia dubia* (cladoceran), *Lymnaea stagnalis* (snail) and *Philodina rapida* (rotifer)	C	Ca^{2+}, H^{+}	DOC and total CO_2	Analysed using multi-linear regression ana-lysis; cross-species modelling of invertebrate chronic Pb toxicity using *C. dubia* seems inappropriate	Esbaugh et al. (2012)
Pb	*Ceriodaphnia dubia*	C		Water hardness, DOM, NOM, DOC (humic acid), pH, alkalinity ($NaHCO_3$)	Hardness did not protect against chronic Pb toxicity; HA and increased alkalinity offered protection but low pH increased the toxicity. A chronic Pb BLM as an alternative approach to hardness-based regulation was recommended	Mager et al (2011b)
Pb	*Pimephales promelas* (fathead minnows)	C		Water hardness, DOC (humic acid)	Only DOC offered protection again Pb accumulation and changes of mRNA expression. Data helped to develop a new chronic Pb BLM for future environmental monitoring and regulatory strategies	Mager et al. (2008).
Sc	*Chlamydomonas reinhardtii*	A	H^{+}	pH	BLM can be used to predict trivalent ion (e.g. Sc) at pH below 6.5 but not above due to transmembrane transport of undissociated Sc hydroxo-complexes	Cremazy et al. (2013)

Metal(s)/ Metal-loid(s)	Test organism(s)	Chronic/ acute expo-sure (C/A)	Cations	Other ligands / factors	Notes	Reference
Tl	*Chlorella sp.*, *Synechococcus leopoliensis*, *Brachionus calyciflorus*	A	K^+, Na^+, Mg^{2+}, Ca^{2+}	Trace metals (Cu, Co, Mo, Mn, Fe and Zn)	BLM successfully predicted the competitive interaction between Tl^+ and K^+; similar amount of K also suppressed toxicity to *S. leopoliensis* and *B. calyciflorus*; absence of trace metals increases Tl uptake and decreased the effect of K^+. K^+ should be considered in predicting biogeochemical fate of Tl in the aquatic environment	Hassler et al. (2007)
Zn	*Fundulus heteroclitus* and *Kryptolebias marmoratus* (killifish)	A	Ca^{2+}	Salinity (estuarine and marine systems)	Zn toxicity decreases as salinity increases	Bielmyer et al. (2012)
Zn		A + C	Ca^{2+}, Mg^{2+}, Na^+, H^+		Proposal of a unified BLM that can predict both acute and chronic toxicity over a range of Zn bioavailabilities	DeForest and Van Genderen (2012)
Zn	*Lymnaea stagnalis* (snail), *Brachionus calyciflorus* (rotifer)	C	Ca^{2+}, H^+	DOC	Chronic Zn model developedfor *Daphnia magna*was used to predict bioavailability of Zn in the mollusc *L. stagnalis* and the rotifer *B. calyciflorus*	De Schamphelaere and Janssen (2010)
Zn	*Oncorhynchus mykiss* (rainbow trout), *Pimephales promelas (fathead minnows)*, *Daphnia magna*	A	Na^+. Mg^{2+}, Ca^{2+},	OH^-, Cl^-, pH, water hardness	Development and application of a Zn BLM; the BLM described well the Zn complexation and Zn-H^+ competition	Santore et al. (2002).

Metal(s)/ Metal-loid(s)	Test organism(s)	Chronic/ acute expo-sure (C/A)	Cations	Other ligands / factors	Notes	Reference
Zn	*Daphnia pulex*	A	Ca^{2+}, Na^{+}, Mg^{2+}, K^{+}, H^{+}	DOC, soft water	Zn BLM was modified to predict acute Zn toxicity on *D. pulex* in soft water; increasing concentrations of DOC or Ca^{2+} (and Mg^{2+} to a lesser degree) had a protective effect	Clifford and McGeer (2009)
Zn	*Daphnia magna*	C	Ca^{2+}, Na^{+}, Mg^{2+},H^{+}		BLM developed to predict chronic Zn toxicity for *D. magna*	Heijerick et al. (2005)
Zn	*Daphnia magna*	A/C			Application of existing Zn BLM to estimate the potential magnitudes and variability of bioavailable Zn in fresh surface water from different regions of the world	Van Genderen et al (2009).
Zn	*Daphnia magna*	A	Ca^{2+}, Na^{+}, Mg^{2+}, K^{+}, H^{+}	Water hardness, DOC	K^{+} and H^{+} did not significantly affect Zn toxicity; BLM developed and validated using 17 media and various pH, water hardness and DOC	Heijerick et al. (2002b)
Zn	*Oncorhynchus mykiss*	C	Ca^{2+}, Na^{+}, Mg^{2+}, H^{+}		The developed BLM predicts chronic effect concentrations with an error of less than a factor of 2 in most cases	De Schamphelaere and Janssen (2004b)
Zn	*Pimephales promelas (fathead minnows)*	A	Ca^{2+}, Mg^{2+}, Na^{+}	DOM, DOC, Cl-	BLM over predicted Zn toxicity in water containing <1 mg DOC/L; the current composite-species BLM for Zn for fathead minnows should be modified	Bringolf et al. (2006)

Metal(s)/ Metal-loid(s)	Test organism(s)	Chronic/ acute expo-sure (C/A)	Cations	Other ligands / factors	Notes	Reference
Zn	*Pseudokirchneriella subcapitata*	A	Ca^{2+}, Na^{+}, Mg^{2+},H^{+}		BLM can be used to predict Zn toxicity in the green alga but need to take into consideration pH and effects of test medium	Heijerick et al (2002a)
U	*Ceratophyllum demersum (*freshwater macrophyte*)*	A	Ca^{2+}, Mg^{2+}		U toxicity is hardness dependent; this finding should be used in guidelines in absence of a U specific BLM	Markich (2013)
U	*Chlamydomonas reinhardtii*	A	Ca^{2+}	CO_3^{2-}, PO_4^{3-}, OH^{-}, NOM, EDTA	No evidence for the transport of intact UO_2^{2+} complexes. BLM was used to correlate the free UO_2^{2+} ion concentration and U uptake	Fortin et al (2004)

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